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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,186	09/21/2007	Rudolf Brenneisen	8588-US	3801

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Nestle HealthCare Nutrition
12 Vreeland Road, 2nd Floor, Box 697
Florham Park, NJ 07932

EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
11/24/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdepartment@rd.nestle.com
athena.pretory@rd.nestle.com

Office Action Summary	Application No.	Applicant(s)	
	10/580,186	BRENNEISEN ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-24,26-33 and 36-47* is/are pending in the application.

4a) Of the above claim(s) *1-9,29-33,36,37 and 41-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12-24,26-28,38-40 and 45-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response after Non-final office action filed on September 15, 2010 is acknowledged. Claims 1-10, 12-24, 26-33 and 36-47 are pending in this application. Applicant elected with traverse of Group 3 and the election of species γ-L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide as the γ-glutamyl peptide, skim milk powder as the calcium source, maltodextrins as the carbohydrate, omega-6 polyunsaturated fatty acid source as the fat source, soy bean derived protein as the nitrogen source, Vitamin A as the vitamin, potassium as the mineral, gum Arabic as the fiber, vegetable flavors as the flavor, and Allium cepa as the Allium, and further elected γ-glutamyl-alkyl-cysteine sulfoxide as the γ-glutamyl-peptide, osteoporosis as the disease, calcium chloride as the calcium source, carbohydrate as the energy source, maltodextrins as the carbohydrate, vitamin D as the vitamin on November 02, 2009. The traversal was not found persuasive, and the restriction was deemed proper and was made FINAL in the previous office action. There were inconsistencies between the elected species filed on August 11, 2009 and November 02, 2009. For the purpose of this examination, the election of species filed on November 02, 2009 was examined. Search was conducted on the elected species, and prior art was found. A prior art WO 98/50054 A1 teaches the other nonelected species. Therefore, election of species was withdrawn in the previous office action. Claims 1-9, 33, 36-37 and 41-44 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 29-32, previously drawn to a γ-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide by fractionation of an hydrophilic, ethanolic extract of Allium have

been amended to method claims. Therefore, Claims 1-9, 29-33, 36-37 and 41-44 remain withdrawn from consideration, as being drawn to nonelected invention. Claims 10, 12-24, 26-28, 38-40 and 45-47 are examined on the merits in this office action.

1. This application contains claims 1-9, 29-33, 36-37 and 41-44 drawn to an invention nonelected with traverse in the reply filed on November 02, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Maintained Rejection

35 U.S.C. 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 10, 12-24, 26-28, 38-40 and 45-47 remain rejected under 35 U.S.C. 102(b) as being anticipated by Muhlbauer (WO 98/50054, filed with IDS) as being evidenced by Kuttan et al (Biochemistry, 1974, 13(21): 4394-4400, filed with IDS) and as evidenced by Wetli et al (J. Agric. Food Chem., 2005, 53(9): 3408-3014, abstract only provided in the previous office action and full article provided herein).

4. Muhlbauer reference teaches a nutritional composition comprising all of the active components of instant claims (see throughout the reference, Claims 5-20), meeting the limitation of instant claims 10 in part, 38 and 45. The reference teaches that the nutritional or pharmaceutical compositions containing a plant extract or concentrate selected from the group consisting of allium, eruca, petroselinum and brassica extracts or concentrates (see abstract and p. 2, last paragraph). The reference teaches that the composition is useful for the treatment of diseases or conditions which are characterized by increased bone resorption, osteoporosis (see abstract). The reference teaches that the term allium refers to the genus allium and includes for example any member of the botanical species Allium cepa (onion), Allium ascalonium and so on, and indicates that the preferred extract is from Allium cepa (see p. 3, 2nd paragraph, see p. 4, 6th paragraph). The onion extracts and concentrates are prepared from the whole eatable part of the vegetable (see p. 3, 3rd paragraph). The reference teaches that the extract and concentrates of the above-mentioned plants or vegetables may be in liquid form or in solid form such as in granulate or powder form (see p. 5, 1st paragraph), meeting the limitation of claims 22-23. The reference teaches that suitable methods of obtaining extracts of the above-mentioned plants or vegetables are known in the art…by extracting the fresh cut or dried plants or vegetables or the respective roots, fruits or seeds thereof for example with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents…ethanol (see p. 5, 3rd paragraph). Further, Example 4 at page 16, explicitly teaches ethanol/water extraction. As evidenced by Kuttan et al, γ-L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide

isolated from sandal (Santalum album L.) is the same as the protein isolated from onion (Allium cepa) (see abstract). The reference teaches that γ-L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide is in aqueous solutions, water (see p. 4396, right column, "CD Absorption"). Therefore, the ethanolic extract of allium cepa of the reference would inherently comprise the γ-L-glutamyl-trans-S-l-propenyl-L-cysteine sulfoxide of the instant claims. The reference teaches that the extract may be used in liquid form, particularly in aqueous form, or in solid form, granulate or powder form. If the extracts in liquid form, it has a solid contents of for example from 1 to 25% by weight, preferably from 2 to 20% by weight and most preferred from 2 to 15% by weight (see p. 6, 2nd paragraph).

The reference teaches that the subject to be treated is an adult person a satisfactory inhibitory effect on bone resorption is, in general obtained with compositions formulated to allow a daily administration of 0.1 to 20 grams, preferably 0.2 to 15 grams and most preferred 0.4 to 10 grams of allium, petroselinum, brassica and/or eruca concentrate or extract (see p. 6, 2nd paragraph). The reference further teaches that suitable nutritional compositions comprising the plant/vegetable extracts comprise at least one (a) plant/vegetable extract or concentrate from allium, (b) a calcium source, and (c) at least one energy source selected from carbohydrate, fat and nitrogen sources, and Vitamin D (see p. 6, last paragraph, claim 5), meeting the limitation of instant claims 10, 12, 38 and 45. Since the nutritional composition comprises the same active compound, this would inherently have the same functionality and characteristics of instant claims 38 and 45. The reference teaches that from approximately 0.1 to 40%,

preferably from approximately 3 to 25% of plant/vegetable extract or concentrate component (a) (see p. 6, last paragraph); calcium source such as calcium chloride or skim milk and the calcium source (b) is in one unit dosage from about 100 mg to 1000 mg, preferably 200 mg to 700 mg or from approximately 1 to 60 %, preferably from approximately 5 to 50% of calcium component (b) (see p. 7, 1st and 2nd paragraph); suitable carbohydrate sources include for example maltodextrins, starch, lactose, glucose (see p. 7, 3rd paragraph); suitable fat sources include omega-6 polyunsaturated fatty acid (see p. 7, 4th paragraph); suitable nitrogen sources such as soybean derived proteins (see p. 8, 4th paragraph), meeting the limitation of claims 14-17 and 19. The reference teaches that the nutritional composition comprise from approximately 0.1 % to 98.9%, preferably from approximately 1 to approximately 95% of energy source (p. 9, 1st paragraph), further meeting the limitation of claim 19. The reference teaches that the carbohydrate source provides for 30 to 70% of the total energy supply, the nitrogen source for 5 to 45 %, and the fat source for 0.1 to 15% of the total energy supply (see p. 9, 2nd paragraph), meeting the limitation of instant claim 18. Further, the reference teaches that the nutritional formulation may comprise other nutritionally acceptable components such as vitamins (see p. 10, 1st paragraph), meeting the limitation of instant claim 20. The reference teaches that the supplement comprises energy sources in an amount supplying from 50 to 1500 kcal/day (see p. 11, 2nd paragraph, see claim 16), meeting the limitation of instant claim 21. The reference teaches that the nutritional formulation is formulated in any form suitable for enteral administration, in aqueous form or in powder or granulate form, whereby the powder or granulate is conveniently added

to water prior to use (see p. 11, 1st and 2nd paragraphs), meeting the limitation of claims 24 and 26. Additionally, the reference teaches dragee, table, capsule, sachet or suppository compositions (see p. 12, 3rd paragraph, see claim 20), meeting the limitation of instant claims 27-28.

Furthermore, the reference teaches that 250 mg freeze-dried onion extract are obtained for each g of dry whole onion, and the onion extract (0.017, 0.17, 1.7 mg onion extract/ ml medium) inhibited osteoclast-mediated resorption (see column 12, lines 1-9). As evidenced by Wetli et al, the molecular mass of gamma-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide is 306 Da (see abstract). The onion extract at 0.017 mg/ ml would yield 55.5 μM effective dose; at 0.17 mg/ml would yield 555.5 μM effective dose; at 1.7 mg/ml would yield 5.55 mM effective dose, Meeting the limitation of instant claims 39-40 and 46-47. Therefore, the reference anticipates instant claims 10, 12-24, 26-28, 38-40 and 45-47.

Response to Applicant's Arguments

5. Applicant argues that "Applicant has surprisingly found that the active constituent of allium responsible for the bone resorption inhibiting effect may be found in a hydrophilic, ethanolic extract of allium such as allium cepa." Applicant argues that "Muhlbauer fails to disclose or suggest nutritional and pharmaceutical compositions, respectively, comprising a γ-glutamyl-peptide selected from the group consisting of γ-glutamyl-alkyl-cysteine sulfoxide, γ -glutamyl-alkenyl-cysteine sulfoxide, and combinations thereof, a carrier, and a fat source as required, in part, by independent claims 10 and 24. Instead Muhlbauer is entirely directed to plant extracts for the

treatment of increase bone resorption." Applicant further argues that "Muhlbauer also fails to disclose or suggest a method of obtaining a γ-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide by fractionation of an hydrophilic, ethanolic extract of Allium, the method comprising the steps of obtaining an hydrophilic, ethanolic extract of Allium cepa, separating saccharides from fraction A, further separating saccharides from fraction A1, and further frantionation by semi-preparative reversed-phase HPLC (SP-RP-HPLC)." Applicant further argues that "Kuttan and Weil fail to disclose or suggest nutritional and pharmaceutical compositions, respectively, comprising a γ-glutamyl-peptide selected from the group consisting of γ-glutamyl-alkyl-cysteine sulfoxide, γ-glutamyl-alkenyl-cysteine sulfoxide, and combinations thereof, a carrier, and a fat source, in part, by independent claims 10 and 24. Kuttan and Weil also fail to disclose or suggest method of obtaining a γ-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide by fractionation of an hydrophilic, ethanolic extract of Allium, the method comprising the steps of obtaining an hydrophilic, ethanolic extract of Allium cepa, separating saccharides from fraction A, further separating saccharides from fraction A1, and further frantionation by semi-preparative reversed-phase HPLC (SP-RP-HPLC)."

6. Applicant's arguments have been fully considered but have not been found persuasive. For the record, Wetli reference was used, and not Weil reference as in Applicant's remarks. The reference teaches all of the active components of instant claims. Muhlbauer reference teaches that the nutritional or pharmaceutical compositions containing a plant extract or concentrate selected from the group consisting of **allium**, eruca, petroselinum and brassica extracts or concentrates. The reference teaches that

the composition is useful for the treatment of diseases or conditions which are characterized by increased bone resorption, osteoporosis. The reference teaches that the term **allium** refers to the genus allium and includes for example any member of the botanical species **Allium cepa (onion), Allium ascalonium** and so on, and indicates that the preferred extract is from **Allium cepa**. The reference teaches that the extract and concentrates of the above-mentioned plants or vegetables may be in liquid form or in solid form such as in granulate or powder. The reference teaches that suitable methods of obtaining extracts of the above-mentioned plants or vegetables are known in the art…by extracting the fresh cut or dried plants or vegetables or the respective roots, fruits or seeds thereof for example **with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents…ethanol**. Example 4 at page 16, explicitly teaches ethanol/water extraction. The instant specification discloses that "The active constituent of allium responsible for the bone resorption inhibiting effect, may be found in an hydrophilic, ethanolic extract of allium such as Allium cepa" (see paragraph [0012] of instant specification US 2008/0194492). Both Kuttan and Wetli references were provided as evidence to show that γ-glutamyl peptide is isolated from Allium cepa. Kuttan et al teach that γ-L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide isolated from sandal (Santalum album L.) and this is the same as the protein isolated from onion (Allium cepa) (see abstract). The reference teaches that γ-L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide is in aqueous solutions, water (see p. 4396, right column, "CD Absorption"). The reference teaches the same water (hydrophilic)/ethanolic extract as the instant specification.

Therefore, the water/ethanolic extract of allium cepa of the reference would inherently comprise the γ-L-glutamyl-trans-S-l-propenyl-L-cysteine sulfoxide of the instant claims. Therefore, the reference anticipates instant claims 10, 12-24, 26-28, 38-40 and 45-47.

In regards Applicant's argument that "Muhlbauer, Kuttan and Weil fail to disclose or suggest to a method of obtaining a γ-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide by fractionation of an hydrophilic, ethanolic extract of Allium, the method comprising the steps of obtaining an hydrophilic, ethanolic extract of Allium cepa, separating saccharides from fraction A, further separating saccharides from fraction A1, and further frantionation by semi-preparative reversed-phase HPLC (SP-RP-HPLC)" the claims drawn to the method claims (claims 29-33, 36-37, 41-44) have been withdrawn from further consideration, as being drawn to nonelected elections. Therefore, these claims were not under examination, and thus, the argument is moot.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Primary Examiner, Art Unit 1654